

Major complications after radiofrequency ablation for liver tumors: Analysis of 255 patients

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Abstract

AIM: To investigate the major complications after radiofrequency ablation (RFA) for the treatment of liver tumors and analyze possible risk factors that precipitate these complications.

METHODS: From March 2001 to April 2008, 255 patients with liver tumors (205 male, 50 female; age range, 18-89 years; mean age, 56.0 years) who received RFA were enrolled in this study. Of these patients, 212 had hepatocellular carcinoma, 39 had metastatic liver tumors and four had cholangiocellular carcinoma. One hundred and forty eight patients had a single tumor, and 107 had multiple tumors. Maximum diameter of the tumors ranged 1.3-20 cm (mean, 5.1 cm). All patients were treated with a cooled-tip perfusion electrode attached to a radiofrequency generator (Radionics, Burlington, MA, USA). RFA was performed *via* the percutaneous approach ($n = 257$), laparoscopy ($n = 7$), or open surgical treatment ($n = 86$). The major complications related to RFA were recorded. The resultant data were analyzed to determine risk factors associated these complications.

RESULTS: Among the 255 patients, 425 liver tumors were treated and 350 RFA sessions were performed. Thirty-seven (10%) major complications were observed which included 13 cases of liver failure, 10 cases of hydrothorax requiring drainage, three cases

of tumor seeding, one case of upper gastrointestinal bleeding, one case of intrahepatic abscess, one case of bile duct injury, one case of cardiac arrest, and five cases of hyperglycemia. Seven patients had more than two complications. Liver failure was the most severe complication and was associated with the highest mortality. Eleven patients died due to worsening liver decompensation. Child-Pugh classification ($P = 0.001$) and choice of approach ($P = 0.045$) were related to post-treatment liver failure, whereas patient age, tumor size and number were not significant factors precipitating this complication.

CONCLUSION: RFA can be accepted as a relatively safe procedure for the treatment of liver tumors. However, attention should be paid to possible complications even though the incidences of these complications are rare. Careful patient selection and the best approach choice (percutaneous, laparoscopy, or laparotomy) will help to minimize the incidence and morbidity rate of complications which occur after RFA.

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Key words: Complication; Hepatocellular carcinoma; Metastatic liver tumor; Radiofrequency ablation; Liver failure

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INTRODUCTION

Hepatocellular carcinoma (HCC) and metastatic liver tumors are the two most common malignant tumors of liver. In most cases hepatectomy is the best curative treatment option^[1,2]. However, there are some factors that limit the use of surgical resection. Therefore, alternative techniques such as percutaneous ethanol injection (PEI), microwave therapy, radiofrequency

ablation (RFA), laser therapy, and transarterial chemoembolization (TACE) have been used for the treatment of hepatic malignant tumors^[3-5]. Among these techniques, RFA is performed more widely than the others because it results in large coagulated necrosis of the tumor, requires fewer treatment sessions, and achieves higher survival rates^[6-8]. Thus RFA would be more beneficial to patients than other non-resectional techniques.

Although RFA is considered a relatively safe and minimally invasive technique, it may induce severe complications. The trade-off between the risks and benefits must be considered. Some major post-RFA complications, such as hepatic failure, intraperitoneal bleeding, hepatic abscess, bile duct injury, tumor seeding, and gastrointestinal perforation have been reported^[9-11]. The estimated range of mortality rate is 0.1%-0.5%, while the major complication rate is 2.2%-3.1%^[12]. A better understanding of the pertinent complications which may occur post-treatment is the key to successful RFA treatment.

Since 2001, we have used RFA to treat patients with HCC or liver metastases. Despite its promising therapeutic effects, RFA has resulted in a number of major complications. In the present study, major complications resulted from RFA procedures during a 7-year-study in a single center have been retrospectively analyzed, and the possible risk factors precipitating these complications were determined.

MATERIALS AND METHODS

Patients

From March 2001 to April 2008, 255 patients with liver tumors (205 male, 50 female; age range, 18-89 years; mean age, 56.0 years) who received RFA were enrolled in this study. Patient characteristics are described in Table 1. Of these patients, 212 had HCC (including 48 cases of recurrent nodules after hepatectomy and five cases of HCC rupture hemorrhage), 39 had liver metastases and four had cholangiocellular carcinoma. One hundred and seventy five patients had chronic liver diseases, of which 168 patients were hepatitis B virus carriers, five patients were hepatitis C virus carriers, and two patients had schistosomiasis liver cirrhosis. Based on Child-Pugh classification, 231 patients (90.6%) were considered as class A, 22 patients (8.6%) as class B, and two patients (0.8%) as class C. Alpha fetoprotein (AFP) serum assays were performed in all patients: 88 patients had normal AFP levels; 92 patients had levels between 5 and 400 ng/mL; and another 75 patients displayed AFP levels of more than 400 ng/mL.

Before treatment, all patients were examined by abdominal ultrasonography, computed tomography (CT) or magnetic resonance imaging (MRI). The location of tumors was defined according to Couinaud's nomenclature. There were 148 uninodular cases and 107 multinodular cases. In 192 patients, we performed RFA only once. In the remaining patients, RFA was

Table 1 Characteristics of patients, tumors and treatment approach (mean ± SD)

Patients and tumor characteristics	Value
No. of patients	255
Median age (yr)	56.0 ± 13.2 (range, 18-89)
Gender (male/female)	205/50
Disease (HCC/MHC/CCC)	212/39/4
Background liver disease (HBV/HCV/ no infection)	168/5/82
Patients with liver cirrhosis <i>n</i> (%)	172 (67.5)
Portal vein invasion (no/yes)	25/230
Alphafetoprotein (0-5/5-400/> 400 ng/mL)	88/92/75
Child-Pugh classification (A/B/C)	231/22/2
ALT (U/L)	47.6 ± 2.5
AST (U/L)	54.7 ± 3.0
Total bilirubin (μmol/L)	27.4 ± 7.1
Serum albumin (g/L)	38.9 ± 0.3
Tumor stage	425
Number of tumors (uninodular/multinodular)	148/107
Size of tumor (cm)	5.1 ± 3.4 (range, 1.3- 20)
Diagnosis (histopathologic/clinical)	215/210
Treatment	350
Choice of approach (percutaneous/ laparoscopy/laparotomy)	257/7/86
Combination with TACE or PEI (+/-)	61/194

performed twice or more due to hepatic recurrence. There were 425 treated tumor nodules in total. The median diameter of the nodules was 5.1 cm (range, 1.3-20 cm), with 174 three centimeters or smaller, 142 between 3.1 and 5 cm, and 109 larger than 5 cm.

The diagnosis of liver tumors was based on histopathological findings of specimens (129 patients, 50.6%). The remaining tumors (126 patients, 49.4%) were diagnosed based on typical CT or MRI findings and tumor markers.

All the patients had contraindications to hepatectomy due to advanced age, associated diseases, severe liver dysfunction, inappropriate location of the tumor, or refusal to undergo the surgical procedure. Before performing RFA, all patients were informed and signed the consent forms.

Technique

A cool-tip needle radiofrequency system (Radionics, Burlington, MA, USA) was used in all patients. The system consists of a perfusion pump, electrode pads placed on the patient's skin, and a radiofrequency generator that monitors tissue impedance, electric current, power and temperature. The shaft of the needle has internal channels which allow the needle to be perfused with chilled water to maintain the temperature of the tip below 20°C to prevent charring around the needle tip. The current is automatically adjusted according to the impedance at the needle tip. Each ablation cycle lasts 12 min. Following ablation, the probe tract is cauterized as the RFA needle is withdrawn. Successful ablation usually increases the temperature of the ablated tissue to 60-80°C. RFA was performed depending on the size and localization of the tumor. A single electrode needle was used for patients with liver tumors smaller than 2 cm.

For patients with large tumors (> 2 cm), we performed overlapping ablations to thoroughly eliminate the tumor. The purpose of the treatment was to achieve destruction of the tumor tissue and the 1 cm margin of parenchyma around the lesion. However, for some patients with large HCCs or portal vein tumor thrombosis, RFA was regarded as a palliative treatment.

RFA was performed *via* the percutaneous approach ($n = 257$), laparoscopy ($n = 7$), or by open surgical treatment ($n = 86$). All the procedures were performed by a surgeon and a radiologist with more than 3 years experience in RFA. Whenever possible, RFA was performed percutaneously. A surgical or laparoscopic approach was adopted to treat patients with tumors located near visceral organs such as the stomach, colon, or gallbladder. When tumors were found near the hepatic hilum, cholecystectomy was performed before RFA. If tumors were located directly below the diaphragm, we used artificial pleural effusion to obtain an image of the whole tumor by percutaneous ultrasonography^[13]. Sixty-one patients had undergone combined treatment for liver tumors (PEI or TACE).

The following serologic values including liver function tests and complete blood counts were measured 3 d and 1 wk after treatment. Treatment efficacy was evaluated by contrast-enhanced CT or ultrasonography 4 wk after treatment. Tumors were considered successfully ablated when no region of enhancement was found either in the entire tumor or in a 0.5 cm margin of normal hepatic tissue surrounding the tumor.

Complications

Major complications were defined as those that delayed hospital discharge, threatened the patient's life, or led to substantial morbidity and disability^[14]. These included liver failure, peritoneal hemorrhage, tumor seeding, and collateral thermal damage to adjacent organs. Differentiation among immediate complications (during the maneuver or ≤ 24 h after the procedure), periprocedural complications (within 30 d), and delayed complications is advised^[12]. Complications were identified on the basis of clinical findings, laboratory or imaging examinations during the RFA and post-treatment observation period.

Statistical analysis

Clinical data of all patients were entered prospectively into a computerized database. We analyzed complications individually instead of combining all the data together. The values of the baseline characteristics, which included patient age, disease, Child-Pugh classification (A *vs* B or C), tumor size and number, treatment approach (percutaneous, laparoscopy or laparotomy), mode of RFA (single or overlapping ablation) were assessed by using Logistic regression analysis. $P < 0.05$ in a two-tailed test was considered statistically significant. All data processing and statistical analysis were performed using commercially available software (SPSS for Windows, Version 11.5).

Table 2 Major complications after radiofrequency ablation

Complication	No. of complications	Disease
Hepatic failure	13	HCCs
Thoracic complications	10	8 HCCs, 1 CCC, 1 MHC
Tumor seeding	3	HCCs
Upper gastrointestinal bleeding	1	HCC
Intrahepatic abscess	1	HCC
Bile duct injury	1	HCC
Cardiac complication	1	HCC
Hyperglycemia	5	HCCs

RESULTS

In the 255 patients, 425 liver tumors were treated and 350 RFA sessions were performed (63 patients had more than one session). The mean follow-up period for the entire group was 32.1 mo (range, 2-84 mo). The median overall survival rate was 21.0 mo. Overall cumulative survival rate at 1-, 2-, and 3-year was 63.1%, 43.3%, and 35.7%, respectively. Thirty five (35/350, 10% per session) major complications were found after RFA treatment (Table 2). Seven patients had more than two types of complications and 28 patients (28/225, 12.4% per patient) suffered from major complications which included 13 (3.7%) cases of liver failure, 10 (2.9%) cases of hydrothorax requiring drainage, 3 (0.9%) cases of tumor seeding, 1 (0.3%) case of upper gastrointestinal bleeding, 1 (0.3%) case of intrahepatic abscess, 1 (0.3%) case of bile duct injury, 1 (0.3%) case of cardiac arrest, and 5 (1.4%) cases of hyperglycemia. The complication rate was 4.0%, 0.3% and 5.7% after percutaneous, laparoscopic and intraoperative RFA, respectively. The immediate complications, periprocedural complications and delayed complications were 2.0%, 29.0% and 4.0% among 350 sessions, respectively.

Liver failure was the most severe complication and was associated with the highest mortality. Eleven patients (11/255, 4.3% per patient) died of worsening liver decompensation. The potential risk factors that might contribute to liver failure were analyzed. We found that Child-Pugh classification ($P = 0.001$) and choice of approach ($P = 0.045$) were related to post-treatment liver failure, whereas patient age, tumor size and number did not correlate with this complication. This finding suggested that Child-Pugh classification and choice of approach were independent risk factors for liver function impairment after RFA.

We adopted intraoperative RFA to treat a patient with an HCC located in the right posterior segment close to the right portal vein (8 cm in diameter). We performed overlapping RFA to achieve a complete ablation area, and the ablated frequency was 12 times. A bile leakage occurred 1 wk after the procedure and subsequently resulted in liver abscess. The patient presented with local pain and high fever. Sustained antibiotic therapy and percutaneous ultrasound guided drainage were carried out. The patient also had diabetes mellitus which

made his basic condition fairly poor. Despite aggressive supportive care, the patient succumbed to progressive liver failure and died 5.5 mo after RFA.

Tumor seeding was identified in three patients (0.86%) at 2, 4 and 5 mo after RFA. These seeding foci were located in the subcutaneous tissue of the abdominal wall (two patients) and omentum (one patient). They were treated by surgical resection, High Intensity Focused Ultrasound and RFA, respectively. Of these three patients, two had undergone previous biopsy, two had an AFP level higher than 400 ng/mL, and all had a single tumor that was not near the capsular fibrosa ranging 2-5 cm in diameter. None of these factors were found to be significantly associated with tumor seeding ($P = 0.085$, $P = 0.840$, $P = 0.088$, respectively).

Hydrothorax was found in ten patients. In five of these cases, tumors were located at the dome of the liver. In one patient with a single 2.5 cm diameter subcapsular HCC in segment VI, cardiac arrest occurred during treatment. She was successfully rescued. Other major complications included one case of upper gastrointestinal bleeding and five cases of hyperglycemia. However, these complications did not result in fatal consequences.

DISCUSSION

RFA has gained wide acceptance as a safe alternative to surgery in the management of early HCC and metastatic liver tumors^[15,16]. It produces complete necrosis of the tumor and achieves a satisfactory survival rate with low recurrence rate on long-term follow-up. Despite the benefits, RFA entails some risks as revealed by post-RFA complications. Complications such as liver failure, intraperitoneal bleeding, abscess, bile duct injury, tumor seeding are very serious, and can be life threatening^[10,17,18]. Being well aware of the complications and the choice of treatment method will lead to a more practical application and enable this procedure to be safer and more effective.

There have been some analyses of post-RFA complications which have involved a large series of investigations^[17]. However, the incidence and mortality of post-RFA complications reported in this study were different from previous reports by other groups. This discrepancy may be attributed to the choice of indications and the skills of the operators. In most of these reports, RFA was performed only when the tumor was no greater than 3 cm in diameter and the patient had no portal vein tumor thrombus. However, in our study, patients with advanced HCC also received RFA treatment, which may have resulted in the relatively high incidence of major complications.

RFA is considered an invasive therapy, especially for those patients with insufficient hepatic reserve to tolerate resection. Therefore, the preoperative evaluation of liver parenchymal function after treatment is of great importance. Decompensated baseline function reserve might precipitate transient liver function impairment after RFA and should be closely followed up. Sepsis and liver failure have been reported as the most common causes of death in a multicenter survey^[19]. Koda *et al*^[20]

analyzed the liver laboratory tests and complications after RFA treatment and found that patients with a high pre-treatment Child-Pugh score suffered from long-term deterioration of liver parenchymal function and subsequent serious complications. The conclusion from that study was that patients with a Pugh score \geq eight points would not be good candidates for RFA or TAE-RFA. In our study, the most severe complication was liver failure, which resulted in mortality in 11 patients after treatment. Our findings demonstrated that Child-Pugh classification was related to post-treatment liver failure. This result was consistent with the finding that Child B or C was a risk factor for post-treatment liver failure^[21]. Therefore these patients may not be appropriate candidates for RFA. The choice of approach was another independent risk factor associated with liver failure. Among the 13 patients who experienced rapid hepatic decompensation, 10 were treated with overlapping ablation *via* an open surgical technique. Recently, intraoperative RFA has been performed as an approach to treat liver tumors, particularly for difficult lesions adjacent to the diaphragm, bowel, or gallbladder. Tepel *et al*^[22] pointed out that although intraoperative RFA was a valuable tool in liver surgery, it added invasiveness and technical difficulties to the procedure and might cause severe post-treatment complications^[23]. When these findings are combined with the results from our study, it becomes more obvious that patient selection and choice of approach are the two major factors to consider in order to achieve desirable outcomes similar to those *via* percutaneous RFA.

Bile duct injury is an uncommon severe complication with an incidence of 0.1%-1.0%^[19,24]. Kim *et al*^[25] demonstrated that although bile duct changes were frequent after the RFA of HCC, it was of no clinical significance in most cases. In addition, major complications requiring additional treatment were rare. Cooling of the biliary tract with chilled saline has been used to prevent biliary injury by RFA^[26]. Ohnishi *et al*^[27] reported that the incidence of biliary injury was significantly reduced in the intraductal chilled saline perfusion (ICSP) group compared to that in the control group. Moreover, liver function in the treated patients was also better preserved in the ICSP group 6 mo after RFA.

We performed overlapping RFA *via* an open surgical approach to treat a patient with a tumor located in the right posterior segment near right portal vein. The patient suffered from bile duct injury combined with other complications including liver failure, hepatic abscess and hyperglycemia. This result was consistent with a previous report^[12] where the possibility of bile duct injury was increased if the mass was located in the central portion of the liver and abutted the portal hepatis. Moreover, excessive heating to overcome the "heat sink effect" of hilar large vessels could cause significant damage to the major ducts.

The incidence of needle-track tumor seeding was reported to range from 0%-12.5%^[28,29]. Llovet *et al*^[28] reported that neoplastic seeding was related to subcapsular location, poor differentiation state of the tumor cells and high AFP levels (more than 100 ng/mL). Livraghi

et al.^{30]} pointed out that RFA with a cooled-tip needle was associated with a low risk of neoplastic seeding, and only previous biopsy was significantly associated with tumor seeding. In our study, we found no risk factors precipitating this complication, even though superficial tumor location, tumor biopsy procedure and AFP level were taken into account. It should be acknowledged that the inability to identify independent predictors of tumor seeding was most likely related to the low number of patients who had this complication. It is thought that intraperitoneal bleeding may drive tumor cells outside the hepatic capsule^{128]}. In our study, no bleeding occurred after RFA, which might also contribute to the low incidence of tumor seeding, particularly for subcapsular tumors.

Complications arising from RFA can be divided into two general categories: those related to imaging-guided electrode placement and those related to thermal transmission^{12]}. Most of the complications such as bleeding, abscess, and gastrointestinal perforation might arise due to improper RFA approach and puncture technique. According to our study, several measures to avoid major complications and to achieve satisfactory therapeutic effect should be taken. Firstly, the most effective strategy to minimize complications is careful patient selection. Preoperative evaluation is of great importance. Patients with Child-Pugh classification B or C and tumors close to vital structures require careful consideration. Secondly, the appropriate approach must be chosen according to the patient's condition. RFA may be performed either percutaneously, *via* laparoscopy or laparotomy, by ultrasound guidance. The trade-off between the risks and benefits must be acceptable. Thirdly, because of the potential incidence of post-treatment complications, a physician should know these pertinent complications, detect the complications as early as possible and provide appropriate management.

In conclusion, RFA is effective for patients with liver tumors. However, liver decompensation may rapidly worsen and lead to life-threatening liver failure, especially in patients with Child-Pugh classification B or C. As the procedure can be associated with major complications, a more accurate selection of candidates and approach to RFA treatment is advisable.

COMMENTS

Background

Although surgical therapy for hepatocellular carcinoma is regarded as standard, most patients are not surgical candidates because of poor liver function or other factors. Many methods of local ablation have been developed to control the disease. Among them, radiofrequency ablation (RFA) is one of the most effective. However, some studies have reported severe complications after RFA, such as hepatic failure, tumor seeding and peritoneal hemorrhage.

Innovations and breakthroughs

This study showed that liver failure was the most severe complication after RFA especially in patients with Child-Pugh classification B or C. The authors also suggested that careful patient selection and the best approach choice might help to minimize the incidence and morbidity rate of complications after RFA.

Peer review

The authors showed the major complications after RFA for the treatment of liver tumors and analyzed the possible risk factors. The results of this research might be important for the clinical application of this therapy.

REFERENCES

- Zhou L, Rui JA, Wang SB, Chen SG, Qu Q, Chi TY, Wei X, Han K, Zhang N, Zhao HT. Outcomes and prognostic factors of cirrhotic patients with hepatocellular carcinoma after radical major hepatectomy. *World J Surg* 2007; **31**: 1782-1787
- Shimozawa N, Hanazaki K. Longterm prognosis after hepatic resection for small hepatocellular carcinoma. *J Am Coll Surg* 2004; **198**: 356-365
- Vogl TJ, Zangos S, Balzer JO, Nabil M, Rao P, Eichler K, Bechstein WO, Zeuzem S, Abdelkader A. [Transarterial chemoembolization (TACE) in hepatocellular carcinoma: technique, indication and results] *Rofo* 2007; **179**: 1113-1126
- Mazzanti R, Arena U, Pantaleo P, Antonuzzo L, Cipriani G, Neri B, Giordano C, Lanini F, Marchetti S, Gentilini P. Survival and prognostic factors in patients with hepatocellular carcinoma treated by percutaneous ethanol injection: a 10-year experience. *Can J Gastroenterol* 2004; **18**: 611-618
- Crocetti L, Lencioni R. Thermal ablation of hepatocellular carcinoma. *Cancer Imaging* 2008; **8**: 19-26
- Yan K, Chen MH, Yang W, Wang YB, Gao W, Hao CY, Xing BC, Huang XF. Radiofrequency ablation of hepatocellular carcinoma: long-term outcome and prognostic factors. *Eur J Radiol* 2008; **67**: 336-347
- Lencioni R, Crocetti L. Radiofrequency ablation of liver cancer. *Tech Vasc Interv Radiol* 2007; **10**: 38-46
- Valls C, Ruiz S, Barrau V, Burdío F, Lladó L, Figueras J, Vilgrain V. [Radiofrequency ablation of hepatic tumors] *Radiologia* 2006; **48**: 53-69
- Perkins JD. Seeding risk following percutaneous approach to hepatocellular carcinoma. *Liver Transpl* 2007; **13**: 1603
- Chen TM, Huang PT, Lin LF, Tung JN. Major complications of ultrasound-guided percutaneous radiofrequency ablations for liver malignancies: single center experience. *J Gastroenterol Hepatol* 2008; **23**: e445-e450
- Zavaglia C, Corso R, Rampoldi A, Vinci M, Belli LS, Vangeli M, Solcia M, Castoldi C, Prisco C, Vanzulli A, Pinzello G. Is percutaneous radiofrequency thermal ablation of hepatocellular carcinoma a safe procedure? *Eur J Gastroenterol Hepatol* 2008; **20**: 196-201
- Rhim H. Complications of radiofrequency ablation in hepatocellular carcinoma. *Abdom Imaging* 2005; **30**: 409-418
- Minami Y, Kudo M, Kawasaki T, Chung H, Ogawa C, Inoue T, Sakaguchi Y, Sakamoto H, Shiozaki H. Percutaneous ultrasound-guided radiofrequency ablation with artificial pleural effusion for hepatocellular carcinoma in the hepatic dome. *J Gastroenterol* 2003; **38**: 1066-1070
- Goldberg SN, Charboneau JW, Dodd GD 3rd, Dupuy DE, Gervais DA, Gillams AR, Kane RA, Lee FT Jr, Livraghi T, McGahan JP, Rhim H, Silverman SG, Solbiati L, Vogl TJ, Wood BJ. Image-guided tumor ablation: proposal for standardization of terms and reporting criteria. *Radiology* 2003; **228**: 335-345
- Khan MR, Poon RT, Ng KK, Chan AC, Yuen J, Tung H, Tsang J, Fan ST. Comparison of percutaneous and surgical approaches for radiofrequency ablation of small and medium hepatocellular carcinoma. *Arch Surg* 2007; **142**: 1136-1143; discussion 1143
- Guglielmi A, Ruzzenente A, Valdegamberi A, Pachera S, Campagnaro T, D'Onofrio M, Martone E, Nicoli P, Iacono C. Radiofrequency ablation versus surgical resection for the treatment of hepatocellular carcinoma in cirrhosis. *J Gastrointest Surg* 2008; **12**: 192-198
- Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. *Radiology* 2003; **226**: 441-451
- Giorgio A, Tarantino L, de Stefano G, Coppola C, Ferraioli G. Complications after percutaneous saline-enhanced

- radiofrequency ablation of liver tumors: 3-year experience with 336 patients at a single center. *AJR Am J Roentgenol* 2005; **184**: 207-211
- 19 **Mulier S**, Mulier P, Ni Y, Miao Y, Dupas B, Marchal G, De Wever I, Michel L. Complications of radiofrequency coagulation of liver tumours. *Br J Surg* 2002; **89**: 1206-1222
- 20 **Koda M**, Ueki M, Maeda Y, Mimura KI, Okamoto K, Matsunaga Y, Kawakami M, Hosho K, Murawaki Y. The influence on liver parenchymal function and complications of radiofrequency ablation or the combination with transcatheter arterial embolization for hepatocellular carcinoma. *Hepatol Res* 2004; **29**: 18-23
- 21 **Hoshida Y**, Shiratori Y, Koike Y, Obi S, Hamamura K, Teratani T, Shiina S, Omata M. Hepatic volumetry to predict adverse events in percutaneous ablation of hepatocellular carcinoma. *Hepatogastroenterology* 2002; **49**: 451-455
- 22 **Tepel J**, Hinz S, Klomp HJ, Kapischke M, Kremer B. Intraoperative radiofrequency ablation (RFA) for irresectable liver malignancies. *Eur J Surg Oncol* 2004; **30**: 551-555
- 23 **McGhana JP**, Dodd GD 3rd. Radiofrequency ablation of the liver: current status. *AJR Am J Roentgenol* 2001; **176**: 3-16
- 24 **Shibata T**, Yamamoto Y, Yamamoto N, Maetani Y, Shibata T, Ikai I, Terajima H, Hatano E, Kubo T, Itoh K, Hiraoka M. Cholangitis and liver abscess after percutaneous ablation therapy for liver tumors: incidence and risk factors. *J Vasc Interv Radiol* 2003; **14**: 1535-1542
- 25 **Kim SH**, Lim HK, Choi D, Lee WJ, Kim SH, Kim MJ, Lee SJ, Lim JH. Changes in bile ducts after radiofrequency ablation of hepatocellular carcinoma: frequency and clinical significance. *AJR Am J Roentgenol* 2004; **183**: 1611-1617
- 26 **Stippel DL**, Bangard C, Kasper HU, Fischer JH, Hölscher AH, Gossmann A. Experimental bile duct protection by intraductal cooling during radiofrequency ablation. *Br J Surg* 2005; **92**: 849-855
- 27 **Ohnishi T**, Yasuda I, Nishigaki Y, Hayashi H, Otsuji K, Mukai T, Enya M, Omar S, Soehendra N, Tomita E, Moriwaki H. Intraductal chilled saline perfusion to prevent bile duct injury during percutaneous radiofrequency ablation for hepatocellular carcinoma. *J Gastroenterol Hepatol* 2008; **23**: e410-e415
- 28 **Llovet JM**, Vilana R, Brú C, Bianchi L, Salmeron JM, Boix L, Ganau S, Sala M, Pagès M, Ayuso C, Solé M, Rodés J, Bruix J. Increased risk of tumor seeding after percutaneous radiofrequency ablation for single hepatocellular carcinoma. *Hepatology* 2001; **33**: 1124-1129
- 29 **Jaskolka JD**, Asch MR, Kachura JR, Ho CS, Ossip M, Wong F, Sherman M, Grant DR, Greig PD, Gallinger S. Needle tract seeding after radiofrequency ablation of hepatic tumors. *J Vasc Interv Radiol* 2005; **16**: 485-491
- 30 **Livraghi T**, Lazzaroni S, Meloni F, Solbiati L. Risk of tumour seeding after percutaneous radiofrequency ablation for hepatocellular carcinoma. *Br J Surg* 2005; **92**: 856-858

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